J6666(C)

AF

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to:

"Commissioner for Patents and Trademarks
Alexandria, Virginia 22313-1450"

on SEPTEMBER 15, 2005

Ellen Plotkin
Reg. No. 36,636
Attorney for Applicant(s)

9/15/05
Date of Signature

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant: GRANGER, et al.
Serial No.: 10/007,869
Filed: November 8, 2001
For: STABLE SKIN CARE PRODUCT CONTAINING A RETINOID AND A RETINOID BOOSTER SYSTEM IN A DUAL COMPARTMENT PACKAGE

Group: 1617
Examiner: Shaojia A. Jiang

SEPTEMBER 15 , 2005

REPLY BRIEF FOR APPELLANTS

Commissioner for Patents and Trademarks
Alexandria, Virginia 22313-1450

Sir:

Enclosed herewith are three (3) copies of a REPLY Brief for Appellant.

Please charge any appropriate fee to our Deposit Account No. 12-1155. Any deficiency or overpayment should be charged or credited to this Deposit Account. This authorization is submitted in triplicate.

Respectfully submitted,

Ellen Plotkin
Registration No. 36,636
Attorney for Applicant(s)

(201) 894-2253

E:\data\word\patents\RetinoidBoosters\J6666\16-RepBRIEF.TL9-15-05.doc

J6666(C)

PATENT

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: "Commissioner for Patents Alexandria, Virginia 22313-1450" on SEPTEMBER 15 , 2005

Ellen Plotkin
Reg. No. 36,636
Attorney for Applicant(s)

09/15/05
Date of Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: Granger, et al.
Serial No.: 10/007,869
Filed: November 8, 2001
For: STABLE SKIN CARE PRODUCT CONTAINING A RETINOID AND A RETINOID BOOSTER SYSTEM IN A DUAL COMPARTMENT PACKAGE

Group: 1617
Examiner: Jiang, Shaojia A.

SEPTEMBER 15 , 2005

REPLY BRIEF FOR APPELLANTS

The following are new points of argument raised by the Examiner's Answer and Appellants' arguments in response thereto.

SUMMARY OF CLAIMED SUBJECT MATTER

To the extent the summary is being repeated, it is to emphasize the invention and differences over the prior art in view of the Examiner's Answer.

The invention set forth in independent claim 1 on appeal is directed to a stable skin care product comprising:

a first composition comprising about 0.001% to about 10% of a retinoid selected from the group consisting of retinyl esters, retinol, retinal, and mixtures thereof;

a second composition comprising about 0.0001% to about 50% of at least one retinoid booster selected from the group consisting of CITRAL, CITRONELLOL, COCAMIDE DEA, DAMASCONE, GERANIOL, 18b GLYCERHETINIC ACID, 8 OH QUINOLINE, N LAURY SARCOSINE, LINALOOL, ALPHA IONONE and LINSEED OIL;

a first compartment for storing the first composition, wherein the first compartment keeps the first composition out of contact with oxygen;

wherein the first compartment is made out of aluminum; and

a second compartment for storing the second composition, the first and second compartments being joined together;

thereby **avoiding chemical degradation of said first composition that would be caused by contact with said second composition**.

The independent claims herein are further limited by dependent claims, some of which are directed to: i.e., Claim 18, the booster alpha-ionone from the Table on page 37 of the Specification; i.e., 2, 7 and 12, retinoid combinations with *at least 2 boosters.* Claim 16 is directed to a combination of at least two boosters where one is climbazole and another is selected among alpha-ionone, damascenone and mixtures.

An **unexpected result** as shown in the Specification and Declaration **of Dr. Iobst submitted July 30, 2004 under 37 CFR 1.132** is that the specified retinoid boosters, despite boosting the effect of specified retinoids on the skin, tend to *destabilize* the specified retinoids in the composition. The claimed retinoid boosters are among a specific list that has been demonstrated *with objective evidence on **p 37 of the Specification*** and in the Rule 132 Declaration to de-stabilize retinoids to a greater extent than the retinoids would be unstable in the absence of the boosters**, i.e., there is a greater stability problem**. The 2d column of the Table on **p 37** lists the fold increase in rate of retinol loss compared to retinol without booster. The retinoid/retinoid booster combinations, *both of which are intended for the same skin benefit and to be applied substantially at the same time,* are maintained in separate compartments of a dual compartment package and the retinoid composition is kept out of contact with oxygen to promote its stability against chemical degradation and **to avoid further instability that would be caused by contact with retinoid boosters.**

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Examiner's Answer position notwithstanding, the Declaration of Dr. Iobst under 37 CFR 1.132 was filed on July 28, 2004 in response to a non-final Office Action, and was entered in the record. The Notice of Appeal was filed on May 10, 2005, significantly later and after a final Office Action that had considered the Declaration. A copy of the previously submitted Declaration was included with the Brief in accordance the rules of Appellate practice. Accordingly, the Rule 132 Declaration should be entered and considered as evidence of unexpected results in the present Appeal.

ARGUMENT

The Examiner's Answer fails to address the key inventive aspect of the present invention, i.e., it fails to address the problem and solution to the additional instability of retinoids due to boosters. The Examiner has rejected claims 1-2, 4-7, 9-12, and 14-18 under 35 USC §103 as being unpatentable over Burger et al. (USPN 5,759,556) and Granger 5,716,627 in view of Liu et al. (USPN 5,976,555) and Suares et al. (USPN 5,914,116) and further in view of Remington's Pharmaceutical Sciences (Remington). The details of the rejection appear in the Appeal Brief and in the Examiner's Answer.

The Examiner again admits that the use of a first compartment for storing retinoid kept out of contact with oxygen and the second compartment for storing boosters (e.g., *alpha-ionone)*, and the first and second compartments being joined together; and **avoiding chemical degradation of retinol or retinyl ester in the first composition that would be caused by contact with boosters** (e.g., *alpha-ionone*) in the second composition are not described in the Burger '556 and Granger '627 references. Additionally, above three cited references to not expressly disclose the first compartment made out of aluminum. The Examiner believes that the deficiencies of the Burger and Granger references are cured by the Liu et al. reference which discloses that retinoids are oxidatively unstable; by Suares et al., U.S. Patent No. 5,914,116 which discloses a first and second composition stored in separate containers joined together; and by the Remington reference which discloses the use of aluminum containers in pharmaceutical products. In this regard, the Examiner maintains that the 35 USC §103 rejection is proper and should be made final.

Notwithstanding the Examiner's apparent position to the contrary, it is, again, the Applicants' position that the presently claimed invention is patentably distinguishable from the above-described for at least the following reasons. A Summary of Claimed Subject Matter has been previously presented and is summarized above.

In contrast to the claimed subject matter and as already made of record, the Burger et al. reference, the primary reference, does not even suggest the need for stable cosmetic compositions that attenuate the existing **problems of retinoid stability in the presence of boosters**. There is no teaching whatsoever in the Burger reference to employ anti-oxidants as described in the present invention. The Examiner correctly admits that the Burger and the Granger '627 references do not describe the use of a first compartment for storing retinoid kept out of contact with oxygen, and a second compartment for storing boosters (e.g., alpha-ionone), and the first and second compartments being joined together; and avoiding chemical degradation of retinoid in the first composition that would be **caused by contact with boosters** in the second composition*; and that the first compartment is made of aluminum.* In view of this, the Examiner relies on the Liu et al. and Suares et al. references, and further in view of Remington's. Again, there is no teaching whatsoever in the secondary references that even remotely suggests the need or solution for **stabilizing retinoid compositions in the presence of retinoid enhancing actives** as described in the present invention. Moreover, there is no teaching whatsoever in the combination of references relied on by the Examiner that even remotely suggests that **boosters destabilize retinoids** to a greater degree than retinoids alone would be unstable, and therefore none of the

references, **alone or in combination of any of the five,** teach or suggest a solution, in particular, a dual compartment container made of aluminum as set forth in the claims.

While Applicants do not dispute the disclosure that retinoids are unstable, Liu et al. ***fail to address the specific further instability contributed to retinoids by the presence of boosters***. **Therefore, Applicants respectfully submit,** Liu et al. do not address **the problem to which the present invention is addressed, i.e., alleviating the additional instability contributed by boosters**. (At most, Liu et al. provide a different solution **to a different problem** – i.e. formulating in an emulsion with a specifically defined chemical stabilizer system, but all in one composition.) The **combination** of cited references does not arrive at the subject matter of the present invention as claimed. Although Liu et al. describe a container for storing the composition so that it is out of contact with oxygen, the container is described in combination with a retinoid composition with an emulsifier system and a co-emulsifier alone and does not protect the retinoid from **degradation due to contact with retinoid boosters**.

Further according to the Examiner, Suares et al. (USPN 5,914,116) teaches a a first and second composition stored in separate containers joined together. However, the product of Suares et al. includes a first composition for obtaining a first skin benefit (e.g., Vitamin A palmitate) and a second composition for obtaining a second and

different benefit, "the first and second actives and benefits being different from one another;" and the two compositions are part of a regimen teaching their application at different times of day. See Col. 2, lines 1-5. The Examiner admits that Suares et al. (USPN 5,914,116) does not teach that the first and/or second compartments keep the respective compositions out of contact with oxygen. Neither do Suares et al. teach that the two compartments are made of aluminum, nor that the two compositions aimed at the same skin benefit and intended to be applied at substantially the same time.

As discussed above, Burger et al and Granger et al. are insufficient primary references and the secondary references do not remedy its deficiencies. Furthermore, there is no motivation to combine Burger and Granger with Remington, Suares et al. and Liu et al. Remington at p. 1511 admits, "The choice of containers and closures can have a profound effect on the stability of many pharmaceuticals."

Accordingly, it would not have been obvious to a person of ordinary skill in the art at the time the invention was made to employ two compartments for separately storing retinol or retinyl ester in a first composition and booster in the second composition in order to **stabilize retinoids against the instabilities caused by the presence of boosters**. In particular, as set forth in detail in the Appeal Brief, Claim 16 is Not obvious over the multiple combined references.

Evidence of Unexpected Results Has Been Presented

To demonstrate unexpected results, attention is drawn to the Table on page 37 of the specification as originally filed, as well as the Rule 132 Declaration of Dr. Iobst. The results of the table demonstrate that *alpha-ionone* (*B1 booster)* increases the rate of retinol loss by a factor of 1.3 according to compositions of the present invention. **The data show that all the claimed boosters significantly increase the rate of retinol loss.** According to the accompanying Declaration, retinol is only 2/3 as stable in the presence of citral. **Dr. Iobst states that, based on analysis of the data presented, it is clear that Retinol stability is significantly diminished in the presence of boosters, creating a greater necessity for its stabilization than in the absence of boosters.** Therefore, the presence of the boosters necessitates separate compartments for the two compositions, more so than the cited art. Neither Liu '555 nor Suares, nor any of the many cited references alone or in any combination, even in the slightest way suggest that boosters further destabilize retinoids. In other words, neither Liu '555 nor Suares, nor any of the many cited references alone or in any combination, suggest a way to protect the retinoid from degradation due to contact with retinoid boosters. The claimed invention is clearly not obvious in view of the cited art, and for the reasons above, the 103(a) rejections should be reconsidered and withdrawn. Additionally, Applicants have shown the advantages of employing more than a single booster with respect to increase in CRABPII production. This advantage

is supported by Dr. Iobst's Declaration while demonstrating the instability due to the presence of boosters.

In view of the above, it is again clear that the Examiner has not established a *prima facie* case of obviousness as required under 35 USC §103. When establishing a *prima facie* case of obviousness, it is fundamentally improper to gloss over important and critical claim limitations. The **"invention as a whole"** must be considered, including all limitations of the claimed invention. *In re Boe*, 184 U.S.P.Q. 38, 40 (C.C.P.A. 1974) ("..., all limitations must be considered and that it is error to ignore specific limitations distinguishing over the references"). It is improper to pick and choose pieces of a variety of art to come up with a rejection as done here. There must be some suggestion or motivation for combinations of the references, so as to come up with the claimed invention, which must be viewed as a whole.

Burger fails to disclose climbazole. Burger and Granger fail to disclose the first compartment for storing retinol or retinyl ester kept out of contact with oxygen; and first and second compartments being joined together; and avoiding chemical degradation of retinol or retinyl ester in the first composition. Nor do Burger, Liu and Suares disclose the first compartment made of aluminum. Remington's is cited for storage of pharmaceuticals to address the aluminum container limitation.

The Examiner's position notwithstanding, Applicants respectfully submit that the significant diminution in retinoid stability in the presence of boosters was **not** known and is unexpected over Liu et al. and Suares et al. alone or in any combination with each other or the other cited references. Liu et al. and Suares et al. have nothing to do with boosters. On the other hand, the present invention teaches the need for stabilizing retinoids in the presence of boosters and evidence in the Examples of the Specification and in the Declaration provides objective support for the unobviousness of the present invention.

If fact, none of the references cited in the Office Action teaches or suggests the need or the solution for stabilizing retinoid compositions in the presence of retinoid enhancing actives. Therefore, although dual purpose single formulation cosmetic products have been developed in the cited art, only in hindsight, with the benefit of the disclosure of the present invention, is the need for stable cosmetic compositions that attenuate the existing problems of retinoid stability in the presence of boosters met. There is no suggestion in the cited art that the **further destabilization of retinoids contributed by the presence of boosters** was within the knowledge which was within the level of ordinary skill at the time the claimed invention was made, nor that the knowledge was generally available to one skilled in the art. Even if combined, Applicants respectfully submit that, since the independent claims are in condition for allowance, those claims that depend from them are also in condition for allowance.

An obviousness rejection is proper only when "the subject matter as a whole would have been obvious at the time the invention was made ..." (emphasis added). 35 U.S.C. 103. Applicants respectfully submit that the Office Action has improperly chosen certain aspects of one reference and combined them with aspects of other references, without showing where the motivation is to combine them to come up with the subject matter of the present invention as a whole, within the meaning of 35 U.S.C. 103. Applicants submit that the pending claims are not obvious over the cited references, under 35 U.S.C. 103. Reversal of this rejection is respectfully requested.

The Double Patenting rejection[1] in improper due to the combination of references, and for the reasons stated above. Since references in addition to Applicants' own patents are being used to make the rejection, the present application does not constitute the same invention or obvious modification of the same invention. See Applied Materials Inc. v. Advance Semiconductor Materials America, Inc., 40 USPQ2d 1481 (Fed. Cir. 1996).

While the Examiner states that knowledge of the state of the art is applicable, per In re McLaughlin, the Examiner fails to address stabilization of retinoids in the presence of boosters. The"knowledge" link is missing in the rejections. Moreover, the "knowledge"

link is rebutted by one skilled in the art. See the Declaration of Dr. Iobst. Therefore, one of ordinary skill of the art would not have found it obvious to keep retinoids stable against destabilization contributed by boosters.

CONCLUSION

In view of the above, Appellants submit that a proper rejection under 35 U.S.C. 103 has not been made. Accordingly, reversal of the Final Rejection by the Honorable Board is appropriate and is courteously solicited.

Respectfully submitted,

Ellen Plotkin
Registration No. 36,636
Attorney for Applicant(s)

(201) 894-2253

---

[1] Nevertheless, Applicants have stated their willingness to supply a terminal disclaimer upon indication of allowability of the present claims.